Association of Pregnancy With Coronavirus Cytokine Storm: Systematic Review and Meta-analysis

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Abstract

Background: COVID-19 was first identified in Wuhan, China, in December 2019, spreading to the rest of the globe, becoming a pandemic. Some studies have shown an association between pregnancy status and severe COVID-19 with a cytokine storm,whereas others have shown contrasting results.

Objective: The aim of this study was to examine the relationship between pregnancy status and the clinical COVID-19 severity characterized by the cytokine storm through a systematic review and meta-analysis.

Methods: We searched the Google Scholar, PubMed, Scopus, Web of Science, and Embase databases to identify clinical studies suitable for inclusion in this meta-analysis. Studies reporting pregnancy status and comparing the COVID-19 severity cytokine storm outcome were included. COVID-19 severity characterized by a cytokine storm was described using parameters such as intensive care unit admission, invasive mechanical ventilation, mechanical ventilation, hospital admission, pro- and anti-inflammatory cytokine levels, consolidation on chest computed tomography scan, pulmonary infiltration, extreme fevers as characteristic of a cytokine storm, syndromic severity, higher neutrophil count indicative of a cytokine storm, and severe COVID-19 presentation.

Results: A total of 17 articles including data for 840,332 women with COVID-19 were included. This meta-analysis revealed a correlation between positive pregnancy status and severe COVID-19 with a cytokine storm (random-effects model odds ratio [OR] 2.47, 95% CI 1.63-3.73; P<.001), with a cumulative incidence of 6432 (14.1%) and 24,352 (3.1%) among pregnant and nonpregnant women with COVID-19, respectively. The fixed-effects model also showed a correlation between pregnancystatus and severe COVID-19 with a cytokine storm (OR 7.41, 95% CI 7.02-7.83;P<.001). Considerable heterogeneity was found among all pooled studies (I^2=98%, P<.001). Furthermore, the updated analysis showed substantially low heterogeneity (I^2=29 %, P=.19), and the funnel plot revealed no publication bias. The sub-analysis between single-center and multicenter studies demonstrated similar heterogeneity (I2=72% and 98%, respectively). Sensitivity analysis on each subgroup revealed that pregnancy was significantly related to severe COVID-19 with a cytokine storm from single-center studies (fixed-effects model OR 3.97, 95% CI 2.26-6.95; P<.001) with very low heterogeneity (I^2=2%, P=.42).

Conclusions: Being pregnant is clearly associated with experiencing a severe course of COVID-19 characterized by a cytokine storm. The COVID-19 pandemic should serve as an impetus for further research on pregnant women diagnosed with COVID-19 to map out the salient risk factors associated with its severity.

Keywords: COVID-19; coronavirus; cytokine; cytokine storm; immune response; infectious disease; maternal health; pandemic; pregnancy; pregnant; respiratory; virus.